II. The Restriction Requirement

In order for a restriction requirement to be proper, the following two criteria must be met: (A) the inventions must be independent or distinct as claimed *and* (B) a serious burden is placed upon the Examiner in prosecution of the subject matter. MPEP § 803.

Applicants maintain that the pending claims, and the sequences therein, represent a single unified invention. Claims 1-15 and 25-30 are drawn to enzymatic nucleic acid molecules comprising certain SEQ ID NOs, which specifically cleaves RNA derived from a TERT gene; antisense nucleic acid molecules comprising complementary sequences to certain SEQ ID NOs; and cells comprising these nucleic acid molecules. Claims 16-24 are drawn to methods of inhibiting telomerase enzyme activity comprising the nucleic acid molecules of Group I. A search of both Groups I and II would not place an undue burden on the Examiner, as the method claims are dependent on the claims encompassing enzymatic and antisense nucleic acid molecules.

As to the further restriction of 10 independent sequences for continued examination, under 37 CFR § 1.141 "more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim generic to all the claimed and all the claims to species in excess of one are written in dependent form (§ 1.75) or otherwise include all the limitations of the generic claim." In the instant case, claims 1-5 are directed to enzymatic nucleic acid molecules that specifically cleave RNA derived from a TERT gene, or antisense nucleic acid molecules that are complementary to a portion of a TERT gene sequence. The remaining claims in Group I are directed to various species that fall in the scope of claims 1-5. Given that the pending claims of the invention satisfy the requirements of CFR 1.141, the further restriction to ten sequences is improper.

Despite this, the Office Action asserts that the claims 1, 3-5 and 25-28 are drawn to patentably distinct sequences because the sequences are unrelated. MPEP § 803.04 specifically addresses applications claiming multiple nucleic acid sequences, providing a definition of nucleotide sequences envisioned to fall within its scope. According to the MPEP:

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> "[n]ucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. . . . each such nucleotide sequence is presumed to represent an independent and distinct invention. . . .

(MPEP § 803.04).

In contrast to the above definition, the claims 1, 3-5, and 25-28 do not recite multiple, independent nucleotide sequences. Rather, the claims recite different species of enzymatic and antisense nucleic acid molecules and specifically targeted to TERT gene. Given that the sequences all specifically cleave (or inhibit through antisense interaction) RNA derived from the TERT gene, they are related. Further, given that the sequences are enzymatic or antisense nucleic acid sequences, the claimed nucleic acid molecules do not represent nucleic acid sequences that encode different proteins. In view of the fact that all of the recited sequences are targeted to a single gene and are not nucleotide sequences that encode different proteins, the claimed sequences do not fit the definition of "structurally distinct chemical compounds" used to determine an independent and distinct invention under MPEP § 803.04.

Moreover, with specific regard to the "relatedness" of the sequences, Applicants point out that many of the claimed enzymatic nucleic acid sequences share invariant spans of sequence (for example, 5'-CUGAUGAGGCCGUUAGGCCGAAA-3' for SEQ ID NOs. 2780-3163 and 5559-5568; 5'-CUGAUGAGGCCGUUAGGCCGAAI-3' for SEQ ID NOs 385-1453; 5'-UGAUGGCAUGCACUAUGCGCG-3' for SEQ ID NOs 4233-4610; and 5'-GGCTAGCTACAACGA-3' for SEQ ID NOs. 1832-2779. Please refer to Tables III-VII for support.

The Office argues that each of the sequences are considered to be structurally independent and distinct even though they target the same gene because each of the sequences has a unique nucleotide sequence and each targets a different and specific region of the gene. Although the Office argues that each of the sequences has a unique nucleotide sequence, in fact, each individual sequence shares invariant spans of nucleic acid sequence common to the enzymatic nucleic acid molecules having that particular motif (see above). Accordingly, the pending claims directed to different enzymatic nucleic acid motifs are different species of enzymatic or antisense nucleic acid molecules

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targeted to TERT gene. Each individual species, or motif, contains sequences common to the subspecies of the particular motif. For all of the reasons discussed above, the pending claims do not meet the established criteria regarding sequence restrictions, and thus do not satisfy the requirements of a proper restriction under MPEP § 803.

Furthermore, as noted above, a proper restriction under MPEP § 803 additionally requires that a serious burden is placed upon the Examiner in prosecution of the subject matter. MPEP § 803. Since all of the sequences are directed to the TERT gene, and all of the enzymatic nucleic acid sequences comprise motifs that possess common nucleotide sequence, a serious burden would not be placed upon the Examiner to search the sequences of the pending claims.

Conclusion:

For all of the reasons discussed above, Applicants submit that the sequences encompassed by the pending claims should not be subject to restriction of ten sequences, and that a serious burden would not be placed upon the Examiner in prosecution of the subject matter. Thus, Applicants respectfully submit that the restriction to ten sequences is improper. Accordingly, Applicants respectfully request reconsideration and withdrawal of the restriction requirement as it applies to the claims of the invention, as well as to restriction to ten individual sequences.

If the Examiner believes that a telephone or personal interview would expedite prosecution of the instant application, the Examiner is invited to call the undersigned at (312) 913-0001.

Respectfully Submitted,
McDonnell Boehnen Hulbert & Berghoff

Date: June 14, 2002

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APPENDIX A
Version With Markings to Show Changes Made to Claims

Bold, underline text, **for example**, indicates inserted text
Bracketed, strikethrough text, [~~for example~~], indicates deleted text

IN THE CLAIMS:

1. (Amended) An enzymatic nucleic acid molecule which specifically cleaves RNA derived from a **telomerase reverse transcriptase (**TERT**)** gene, wherein said enzymatic nucleic acid molecule comprises any of the ribozyme sequences [~~defined in tables III, IV, V and VII~~] **identified as SEQ ID NO: 2780-3163, 385-1453, 1454-1831, 5559-5568, 4332, 4471, or 4594**.

3. (Amended) An enzymatic nucleic acid molecule of claim 2, wherein said enzymatic nucleic acid molecule comprises any of the DNAzyme sequences [~~defined in table VI~~]**identified as SEQ ID NO: 1832-2779**.

4. (Amended) An enzymatic nucleic acid molecule which specifically cleaves RNA derived from a TERT gene, wherein said enzymatic nucleic acid molecule comprises sequences that are complementary to any of substrate sequences [~~defined in tables III-VI~~]**identified as SEQ ID NO: 1-384 or 3164-5558**.

5. (Amended) An antisense nucleic acid molecule comprising sequence complementary to any of substrate sequences [~~in Tables III-VI~~]**identified as SEQ ID NO: 1-384 or 3164-5558**.

25. (Amended) The enzymatic nucleic acid molecule of claim[s] 1, wherein said enzymatic nucleic acid molecule comprises any of sequences [~~of table III~~]**identified as SEQ ID NO: 2780-3163**.

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26. (Amended) The enzymatic nucleic acid molecule of claim[s] 1, wherein said enzymatic nucleic acid molecule comprises any of sequences [~~of table IV~~]**identified as SEQ ID NO: 385-1453**.

27. (Amended) The enzymatic nucleic acid molecule of claim[s] 1, wherein said enzymatic nucleic acid molecule comprises any of sequences [~~of table V~~]**identified as SEQ ID NO: 1454-1831**.

28. (Amended) The enzymatic nucleic acid molecule of claim[s] 1, wherein said enzymatic nucleic acid molecule comprises any of sequences [~~of table VII~~]**identified as SEQ ID NO: 5559-5568, 4332, 4471, or 4594**.

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